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Effect of gastrectomy on G-cell density and functional activity in dogs

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INTRODUCTION

Billroth gastrectomy has some advantages of inhibiting acid secretion, low ulcer recurrence and low mortality. However, postoperative complications, such as dumping syndrome and reflux gastritis, often occurred as a result of pylorectomy[1]. To minimize these complications, pylorus-preserving gastrecto my (PPG) had been performed for gastric ulcer with satisfied clinical results. P ositive correlation was not found between ulcer recurrence and serum gastrin level[2]. In this study, we performed distal partial gastrectomy with Billr oth II anastomosis (DPG-BII), pylorus-preserving gastrectomy (PPG) and highly seclective vagotomy (HSV) on dogs and investigated the relationship between dif ferent antrum disposal and gastric acid secrection, serum gastrin level and G-cell density and functional activity.

MATERIALS AND METHODS

Eighteen hybrid adult dogs, with body weight ranging from 10 kg to 20 kg , mean weight 13.9 kg, were randomly divided into 3 groups, and underwent PPG, DPG-BII or HSV respectively. In PPG group, antrum was strictly retain ed within 1.5 cm-2.0 cm and stomach was resected about 40%. DPG-BII, in which stomach was resected about 75%, and HSV were routinely done. After laparotomy biopsy was taken at antrum 2 cm beyond the pyloric sphincter, the first segmental duodenum and jejunum 4 cm beyond Treitz ligamenta, 3 mo after operation, biopsies were done again around the original biopsy sites. Gastric acid secretion was analyzed using neut ralization method (subcutaneous injection of tetra-gastrin 4 μg/kg). Fasting and postprandial serum gastrin levels were measured by radioimmunoassay. The G cell density and its functional activity were determined by immunohistochemical assay using an antigastrin antibody (Zymedco) at a dilution of 1:200 in PBS. G cell density was measured according to the method of Creutzfeldt[3], in which G cell functional activity was divided into 4 grades, as follows: 1+, brown-red cyto plasm, without granule; 2+, minute brown granules, occupied within 1/3 cyto plasm area; 3+, brown granule or clusters occupied, 1/3-2/3 cytopl asm area; 4+, brown-black granules or clusters, above 2/3 cyto plasm area .

RESULTS

Effects of different operative procedures on gastric acid secretion

In DPG-BII, PPG and HSV groups, preoperative basal acid output (BAO) was 1.80 mmol/h, 2.25 mmol/h and 2.19 mmol/h; maximal ac id output (MAO) was 5.19 mmol/h, 4.49 mmol/h and 5.30 mmol/ h, respectively; 3 mo after operation, BAO decreased to 0.48 mmol/h, 0. 98 mmol/h and 0.97 mmol/h; while MAO decreased to 1.04 mmol/h, 1.76 mmol/h and 1.29 mmol/h, respectively. Gastric acid secretion was significantly suppressed by 56%-80%, which sho wed that all of the three operations can effectively inhibit gastric acid secret ion in dogs (Table 1).

Effects of different operative procedure on serum gastrin level

Pre and post-operative fasting and postprandial serum gastrin levels of DPG-BII, PPG and HSV groups are shown in Table 2. In DPG-BII, post-operative fasting and postprandial serum gastrin levels were significantly decre ased ($P<0.05$), the inhibiting rate was 49.7% and 48.4% respectively ; while in PPG, serum gastrin levels were slightly decreased with an inhibiting rate of 25.9% and 24.4%; in HSV, post-operative serum gastrin levels were increased by 65.2% and 54.1%, respectively.

Effects of different operative procedure on G cell density and functional activity

Postoperatively, G cell density increased in all sites checked. The increasing rate in duodenum was about 75.0% and 50.0% in antrum or residual antrum (Table 3). The increase in jejunum had no statistical significance.

Stained by immunohistochemical method, G cell was stained in brown color and there were brown-black granules in cytoplasm, which were the product s of gastrin acted with its antibody and presented as the index of activity of G cell. If 1+

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and 2+ grade cell was taken as normal- or hypofunction, while 3+ and 4+ as hyperfunction, the number of grade 3+ and 4+ G cells as a whole constituted 44% and 60% of the total G cells examined in pre and post-operative specimens respectively, and particularly in duodenum the corresponding postoperativ e date was 63%. It reveals that no matter what procedure of gastrectomy was perf ormed, the post-operative G cell functional activity, especially in duodenum wa s enhanced with statistical significance (Table 4).

Table 1 Effects of different operative procedures on gastric acid secretion

Operation	Group	Preoperation (mmol/h)	Postoperation (mmol/h)	Inhibiting rate (%)
DPG-BII	BAO	1.80 ± 0.25	0.48 ± 0.20[b]	73.7
	MAO	5.19 ± 0.56	1.04 ± 0.19[b]	80.0
PPG	BAO	2.25 ± 0.27	0.98 ± 0.26[a]	56.4
	MAO	4.49 ± 0.34	1.76 ± 0.19[b]	60.7
HSV	BAO	2.19 ± 0.21	0.97 ± 0.26[a]	55.9
	MAO	5.30 ± 0.14	1.29 ± 0.47[b]	75.7

[a]$P<0.05$; [b]$P<0.01$, *vs* preoperation.

Table 2 Effects of different operative procedure on serum gastrin level

Operation	Group	Pre-operation (ng/L)	Post-operation (ng/L)	Changing rate(%)
DPG-BII	fasting	179 ± 104	90 ± 117[a]	↓ 49.7
	postprandial	181 ± 86	94 ± 39[a]	↓ 48.8
PPG	fasting	190 ± 153	144 ± 63	↓ 25.9
	postprandial	239 ± 115	180 ± 47	↓ 24.4
HSV	fasting	100 ± 10	166 ± 75	↑ 65.2
	postprandial	103 ± 48	186 ± 63	↑ 54.1

[a]$P<0.05$, *vs* preoperation.

Table 3 Effects of different operative procedure on G cell density

Operation	Site	Preoperation (cell/field)	Postoperation (cell/field)	Incerasing rate(%)
DPG-BII	Duodenum	23.1 ± 5.0	41.3 ± 4.9[b]	78.9
	Jejunum	1.1 ± 1.1	3.2 ± 3.0	190.4
PPG	Antrum	66.2 ± 2.1	103.3 ± 18.8[a]	56.0
	Duodenum	15.6 ± 5.3	27.1 ± 3.6[a]	74.3
	Jejunum	1.0 ± 4.2	1.1 ± 1.9	11.0
HSV	Antrum	69.8 ± 23.2	103.3 ± 19.3[b]	47.6
	Duodenum	33.7 ± 15.1	60.1 ± 21.5	78.5
	Jejunum	5.5 ± 3.3	17.3 ± 9.2	218.3

[a]$P<0.05$; [b]$P<0.01$, *vs* preoperation.

Table 4 Effects of different operations on G cell function

Operation	Site	Group	1+	2+	3+	4+
DPG-BII	Duodenum	Preoperation	21	142	106	29
		Postoperation	24	73	157	46[b]
PPG	Antrum	Preoperation	32	136	71	61
		Postoperation	23	115	64	98[a]
	Duodenum	Preoperation	50	124	81	45
		Postoperation	24	93	117	68[b]
HSV	Antrum	Preoperation	55	105	84	56
		Postoperation	38	94	73	95[a]
	Duodenum	Preoperation	67	107	74	52
		Postoperation	24	99	81	96[b]

[a]$P<0.05$; [b]$P<0.01$, *vs* preoperation.

DISCUSSION

According to the theory "no acid, no ulcer", anti-acid secretion has been the dominant measure in treating peptic ulcer. For suppressing acid secretion, how to treat the antrum has been a much controversial question in general surger y[4]. Total antrum excision would make the serum gastrin level and gastr ic acid output lowered, which was accompanied with relatively lower ulcer recurr ence; on the other hand, damage of sphincter function resulted in dumping symdro me, reflux gastritis, dyspepsia and even carcinogenesis of residual stomach[1]. Under this condition PPG was presented, which not only removed the ulce r lesion and suppressed gastric acid secretion, but also preserved the sphincter function[5]. Our results showed that all the three proce dures can effectively inhibit gastric acid secretion in spite of the different p ostoperative serum gastrin levels. Clinically, similar results were observed tha t absolute serum gastrin value of patients were all kept within normal limits, regardless their gastrin level decreased or increased after DPG-BII, PPG or HSV[2]. This implied that different disposal of antrum did not obviously affect the inhibition of gastric acid secretion.

Gastric acid secretion is a complex physiological process, which was regulated by several factors, such as vagus nerve, G cell, parital cell and its receptor, some alimentary endocrine substances, gastric mucosal blood supply[6]. Of them any change may inhibit the gastric and secretion and keep it at lower ou tput level. In addition to regulating acid secretion, gastrin has important effe cts on nourishment of gastric mucosa and pancreas[7]. Our results showed that there were many G cells in duodenum and jejunum besides antrum. After operation, the number of G cells in the nongastric tissue increased and their function enhanced, this was not only associated with the gastric acid deplation, but also was demanded by other physiological effects. Therefore it is evidently impossible and unnecessary to eliminate gastrin from serum by operation of peptic ulcer. To some extent, hypergastrinemia subsequent to treatment of peptic ulcer, such as HSV and antiacid drugs, is the main determinant of ulcer healing[8]. It is the key point that how to keep the whole function of sphincter. Fukushima *et al*[5] has discovered that the length of preserved antrum was closely related to the residual stomach function. In our study, the length of preserved antrum was strictly limited within 1.5 cm to 2.0 cm, vomiting, decline of food intake and loss of body weight were not found postoperatively in the animals which suggested that the function of sphincter had been fairly maintained.

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